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Abnormal Head MRI in a Neurologically Normal Boy With Hypomelanosis of Ito

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We report on an 8.5-year-old boy with hypomelanosis of Ito (HI) who has an abnormal MRI of the brain but is neurologically normal. There have been many reports of abnormal brain imaging studies in patients with HI, but all reported patients have had abnormal neurologic findings or symptoms. Our patient has had serial, stable head MRI white matter changes and has remained neurologically normal without any neurologic sequelae. © 1996 Wiley-Liss, Inc.

KEY WORDS: Hypomelanosis of Ito, head MRI

INTRODUCTION

Hypomelanosis of Ito (HI) is a rare neurocutaneous syndrome characterized by areas of skin hypopigmentation in the form of streaks or whorls. Half of patients are reported to have central nervous system (CNS) involvement [Jelinek et al., 1973; Schwartz et al., 1977; Golden and Kaplan, 1986; Pascual-Castroviejo et al., 1988]. In the past few years there has been an increasing number of reports discussing abnormalities found with CNS imaging techniques. All patients reported with abnormal CNS imaging studies have also had various neurologic abnormalities. We report on an 8.5-year-old boy with an abnormal head MRI who is neurologically normal with normal IQ. An abnormal brain MRI may not predict a poor or abnormal neurologic outcome in HI.

CLINICAL REPORT

The patient was a white boy, the 3.6 kg product of an uncomplicated term pregnancy to a 28-year-old $G_3P_1SAB_1$ woman. At birth the boy was noted to have a large head with asymmetry of face and limbs with polysyndactyly. He was evaluated at age 2 weeks and noted to have an OFC of 38 cm (90–95th centile) with weight and length at the 75th centile. He had scaphocephaly with prominence of occiput, right side of the face smaller than left, and right arm and leg smaller in circumference and length than the left. It was not clear at that time if these asymmetries reflected hemihypertrophy or hemiatrophy. He had 6 digits on the right foot with a bifid 5th toe and webbing between the 4th and 5th toes, bilaterally. CT scan showed some prominence of the ventricles and subarachnoid spaces. Skull films were normal. A repeat head CT at 9 months of age was unchanged. The patient was also evaluated by neuro-ophthalmology at 5 months because of orbital asymmetry and was noted to have a refractive error and posterior staphyloma O.D.

The patient was not reevaluated until age 5 years at which time a head MRI showed stable, mild enlargement of the third and lateral ventricles. However, striking white matter abnormalities were apparent in both cerebral hemispheres (Fig. 1A–C). The central and periventricular white matter demonstrated mild hypointensity on T1-weighted images and hyperintensity on proton density and T2-weighted images. The white matter lesions were broad and confluent and without mass effect. Thin bands of alternating signal intensities were identified within the areas of abnormal white matter, seemingly radiating outward from the lateral ventricles. Several small cyst-like lesions were scattered in the central white matter (Fig. 1C). The gyral pattern of the cortex was normal. Also noted was a small right optic nerve. The mother reported that the patient was classified as blind in his right eye, but had otherwise been healthy with normal intelligence. She denied regression of skills or seizures. He had hemiatrophy of the right side of the face and body, downslanted palpebral fissures, nasal tip deviating to the right, as did the chin. He had crowding of teeth and lacked right central and left lateral incisors. The ears were apparently low-set but normal in configuration, with the right ear smaller than the left. There was streaky linear hypopigmentation across the right arm with swirling hypopigmentation involving the right chest and back with a small amount of involvement on the left. There was also streaky hypopigmentation on both legs, more so on the right than left. The mother

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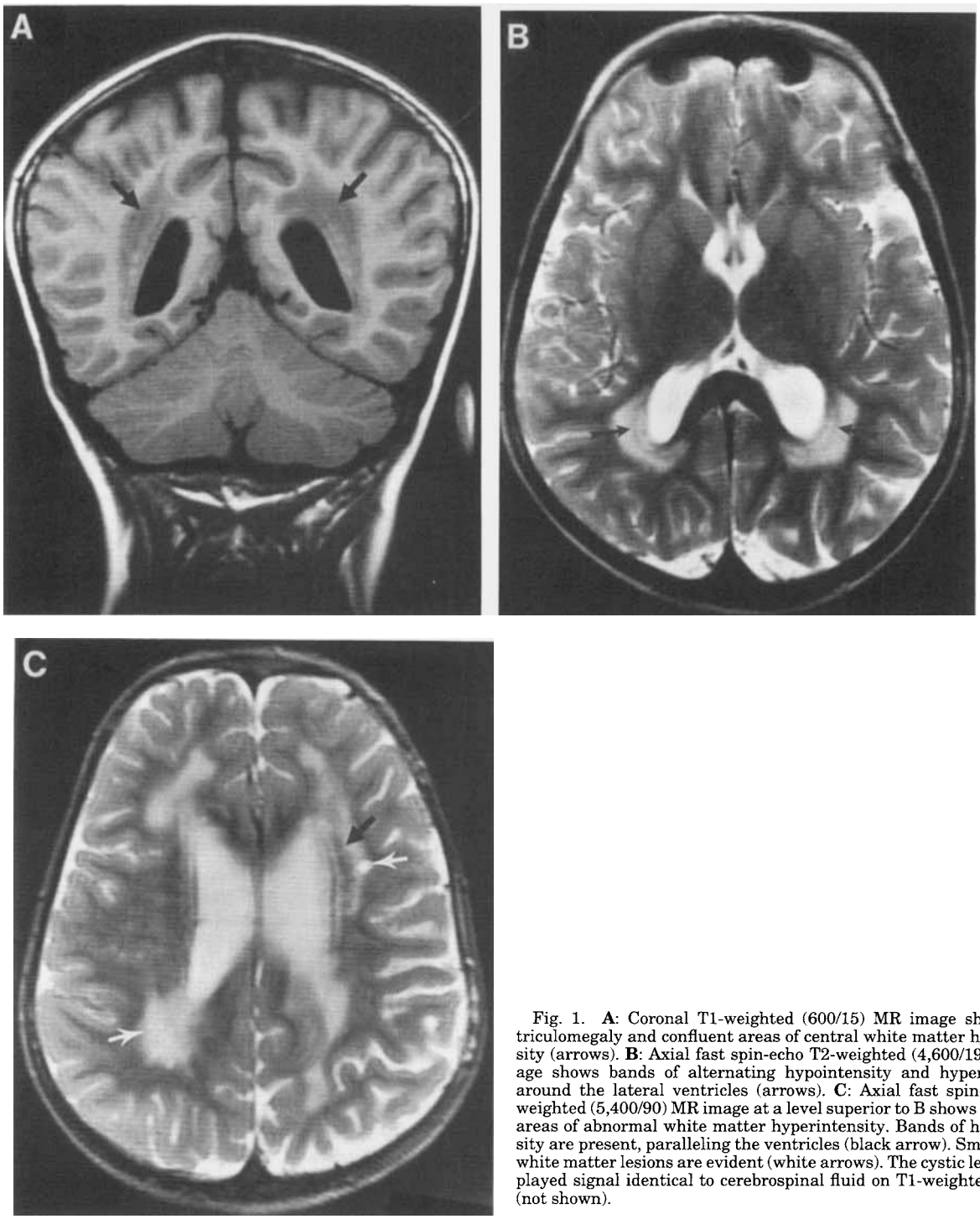

Fig. 1. **A**: Coronal T1-weighted (600/15) MR image shows ventriculomegaly and confluent areas of central white matter hypointensity (arrows). **B**: Axial fast spin-echo T2-weighted (4,600/19) MR image shows bands of alternating hypointensity and hyperintensity around the lateral ventricles (arrows). **C**: Axial fast spin-echo T2-weighted (5,400/90) MR image at a level superior to B shows extensive areas of abnormal white matter hyperintensity. Bands of hypointensity are present, paralleling the ventricles (black arrow). Small, cystic white matter lesions are evident (white arrows). The cystic lesions displayed signal identical to cerebrospinal fluid on T1-weighted images (not shown).

stated the cutaneous changes appeared in the first year of life. The right arm and leg were smaller in circumference than the left, but equal in length. There was no change in the postaxial polysyndactyly noted earlier and the neurologic status was normal. Neurodevelopmental evaluation including IQ testing was normal. The family deferred blood sampling and skin biopsies for chromosomal analysis.

Repeat brain MRI of the patient at age 7 years was unchanged. His hemiatrophy has persisted and the cutaneous changes are still evident and unchanged. His most recent evaluation at age 8.5 years (Figs. 2–4) showed no significant changes and his neurological status was normal, except for poor vision in his right eye. The patient is currently in second grade and doing well academically. He has had delay in some of his

Fig. 2. Face and upper torso of patient, age 8.5 years. Note facial asymmetry, streaky hypopigmentation of right arm, swirly hypopigmentation of chest.

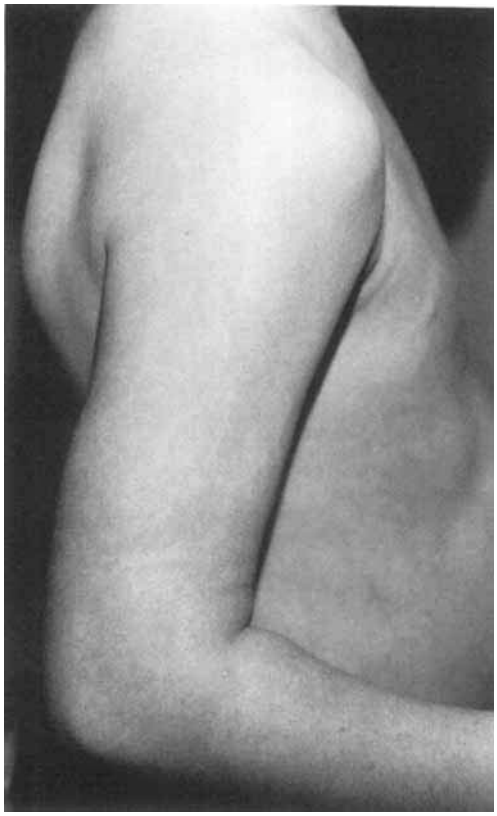

Fig. 3. Patient's right arm; closer view of streaky hypopigmentation.

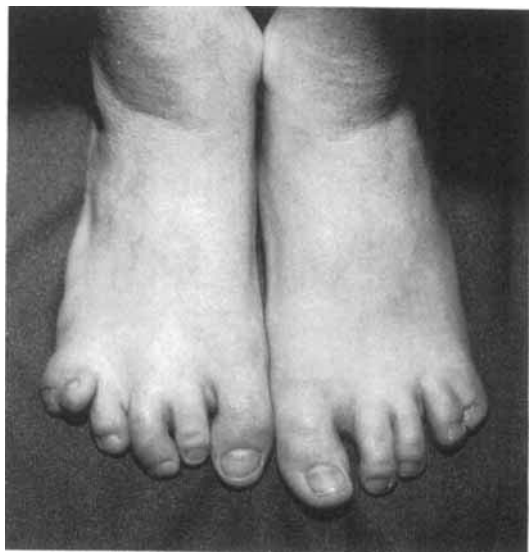

Fig. 4. Patient's feet; note polysyndactyly on the right and syndactyly on the left.

permanent dentition despite normal loss of his primary teeth. He has never had seizures or loss of any skills.

DISCUSSION

HI is a rare but well-described neurocutaneous disorder. Neurological complications and abnormal head imaging studies are also well-described. It is estimated that 50% of patients with HI have neurologic symptoms [Jelinek et al., 1973; Schwartz et al., 1977; Golden and Kaplan, 1986; Pascual-Castroviejo et al., 1988]. Abnormalities include mental retardation, seizures, hypotonia, nystagmus and ataxia. A review discusses neurologically abnormal children, some with abnormal head imaging studies and some with normal neurologic status [Rosemberg et al., 1984; Ardinger and Bell, 1986; Golden and Kaplan, 1986; Pascual-Castroviejo et al., 1988; Bhushan et al., 1989; Federico et al., 1989; Hara et al., 1989; Hashimoto et al., 1990; Williams and Elster, 1990; Åkefeldt and Gillberg, 1991; Malherbe et al., 1993; Zappella, 1993; Kimura et al., 1994]. Central nervous system imaging has demonstrated localized or generalized cerebral atrophy, ventricular enlargement, cerebellar hypoplasia, hypodensity of cerebral white matter, hemimegalencephaly, heterotopia, abnormal neuronal migration, and focal or multifocal areas of prolonged T2 relaxation in the white matter [Ross et al., 1982; Ardinger and Bell, 1986; Dunn et al., 1986; Persico et al., 1988; Bhushan et al., 1989; Glover et al., 1989; Williams and Elster, 1990; Kimura et al., 1994; Tagawa et al., 1994]. Neuropathologic findings have consisted of gray matter heterotopia, pachygyria, atrophy, abnormal cortical lamination in gyri with extensive gliosis, and disordered cortical lamination in nerve cells in the white matter and periventricular regions [Ross et al., 1982]. In our case, the alternating bands of signal just beyond the ventricular margins are suggestive of layers of neurons that were arrested during migration to the cortex (i.e., laminar or band heterotopia).

This same finding appears to be present (although not discussed in the reports) on MR images published in 2 other patients with HI [Bhushan et al., 1989; Williams and Elster, 1990]. The white matter signal abnormalities in our patient, with the smooth lesion margins and lack of involvement of the subcortical white matter, are also similar to images published in 3 patients with this same syndrome [Bhushan et al., 1989; Williams and Elster, 1990; Kimura et al., 1994]. These lesions may represent areas of hypomyelination.

In one case of HI, Ross et al. [1982] reported the pathological finding of a lack of myelination within areas of cerebral white matter that contained gray matter heterotopia. Other explanations for our patient's extensive white matter abnormalities, such as widespread gliosis or demyelination, are unlikely in a neurologically normal patient. While lacking pathologic confirmation, our findings of only thin bands of heterotopia, no cortical dysplasia, and normal neurologic development are in agreement with the observations made by Barkovich and Kjos [1992] in patients with gray matter heterotopia and without HI: they found a highly significant correlation of heterotopia thickness with degree of developmental delay, and of cortical dysplasia with degree of developmental delay. Included in their series were patients with normal development and intelligence; some of them did not develop a seizure disorder until the second decade of life. One 15-year-old subject was asymptomatic. Other asymptomatic patients have been reported to have heterotopic gray matter on either MRI or at autopsy [Smith et al., 1988; Harding, 1992]. The pathologic correlate of the cyst-like lesions has not been reported. Williams and Elster [1990] also observed small periventricular cystic lesions on MR in one case of HI.

Our patient had white matter changes but normal neurologic status. It is possible that other patients with HI who do not have neurologic abnormalities have not had head imaging and so there may be a bias of ascertainment. It is also possible that the lack of involvement of cortex in our patient has contributed to his normal neurologic examination and status. We present this case to suggest that an abnormal head MRI in a patient with HI may not predicate a poor or abnormal neurologic outcome. In cases of HI with mental retardation with or without evidence of CNS white matter disease, the clinical course has been described as nonprogressive [Rosemberg et al., 1984; Malherbe et al., 1993]. The stability of our patient's clinical status as well as head MRI changes has provided some reassurance that the MRI changes may not indicate eventual neurologic involvement. Some authors recommend that an MRI of the brain should be obtained in all patients with HI once the diagnosis is made [Bhushan et al., 1989]. It would provide greater reassurance to the family and ourselves to know of other cases of HI with similar head MRI changes in neurologically symptom-free patients.

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